REFERENCES


Paget's disease of the breast

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Summary

Twenty patients with histologically proven Paget's disease of the breast are reviewed. They represent an incidence of 1.06% of all breast carcinomas seen over a 12-year period in the Bloemfontein academic hospitals. All cases had ductal carcinoma. Clinically, 20% presented with a mass, 20% with nipple disease only and 60% with both lesions. More patients with a mass compared with patients with only nipple disease had positive axillary lymph nodes - 68.7% v. 25%. Cumulative 5-year survival rates showed a 100% survival rate for patients with only nipple disease, and an 83% survival rate for stage I and II disease. All the patients with stage III and IV disease died within the 4-year follow-up period. Nipple (skin) involvement per se did not worsen the prognosis of patients presenting with both a mass and nipple disease. The main predictors of prognosis were tumour size and lymph node involvement. It is suggested that patients presenting with nipple involvement only and/or small T1 lesions close to the nipple could be treated with wide local excision and axillary dissection in discontinuity followed by radiotherapy to the rest of the breast.

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The incidence of Paget's disease of the breast has been reported to be in the range of 1-4% of all breast carcinomas. Although a rare condition, there was much debate and controversy about Paget's disease of the breast in the past, the main issue being its pathogenesis. However, it is now generally agreed that the disease originates in the larger retro-areolar lactiferous ducts of the breast and progresses not only centrifugally in the breast but also towards the nipple-areola complex, and causes the typical clinical picture of nipple-areolar erosion.

Debate and controversy still continue about the best way to treat Paget's disease of the breast. This arose because Paget's disease does not represent a homogeneous disease entity and so different treatment regimens might be possible for subcategories of patients. Clinically, Paget's disease of the breast can present in three different ways: (i) with a mass only; (ii) with both a mass and nipple or skin involvement; and (iii) with nipple-areolar disease only. The different clinical presentations have different prognostic implications. Patients with nipple-areolar disease alone have a very good prognosis with 10-year survival rates of the order of 80-85%. On the other hand, Paget's disease of the breast presenting with a mass behaves like ordinary breast carcinoma. Recently, better understanding of the natural behaviour of breast carcinoma has made less and conservative surgical treatment an acceptable concept. Whether these principles can also be applied to Paget's disease of the breast is unclear.

According to the TNM classification of the American Joint Committee for Cancer Staging and End-Results Reporting (AJCC), a breast carcinoma presenting with a mass and skin (nipple) involvement indicates stage IV disease with a poor prognosis. In contrast in Paget's disease nipple involvement alone has a very good prognosis. This raises the question of what the biological implications of nipple-areolar or skin involvement in Paget's disease of the breast really are. If it could be shown to be unimportant, then the TNM classification could be applied to any mass in Paget's disease of the breast.
regardless of nipple and/or skin involvement and still have prognostic predictability as well as some possible influence on future treatment policy. A study was undertaken to investigate this possibility as well as to ascertain the incidence of the disease in the Bloemfontein academic hospital, the clinical and histological presentation and also to determine whether there are any racial differences that might influence future treatment strategies.

Patients and methods

The records of all patients who attended the breast clinic during the period January 1971 - December 1982 were retrospectively reviewed. There were 20 patients with histologically proven Paget's disease of the breast who represent the study group. Complete clinical, histological and follow-up data were available on the whole group.

The patients were grouped, as described by Kister and Haagensen, in three different categories according to their clinical presentation: (i) a mass only; (ii) a mass with nipple-areolar and/or skin involvement; and (iii) nipple-areolar disease only. These data were also correlated as regards the different race groups. The axillary lymph node status was correlated according to whether a mass was present or not. Using the Life Table analysis method the cumulative 5-year survival rates were determined for the different subgroups.

Utilising clinical and histopathological data, all patients presenting with a mass were then staged according to the AJCC TNM method. In this retrospective staging those patients who presented with skin or nipple involvement, T4 or stage IV according to the AJCC TNM staging method) as well as a mass were graded for T value by tumour size alone (T1 = 1 - 2 cm; T2 = 2 - 5 cm; T3 = 5 cm). The N and M values were determined according to the AJCC TNM method. The different TNM combinations were then calculated to determine the different stages. Again using the Life Table analysis method, the cumulative 5-year survival rates were determined for the differently staged groups. The differences between the race groups were also correlated with the TNM staging of the patients.

The treatment regimens of the patients were retrospectively constructed on the basis of their TNM staging (Table I). All the patients with in situ and stage I lesions were treated by a modified radical mastectomy only. Three patients with stage II disease had operations which were less severe than a modified radical mastectomy and also received radiotherapy. When lymph nodes were involved, adjuvant chemotherapy was given. Most of the patients with stage IV disease were treated by modified radical mastectomy for toilet and debulking purposes. This operation was only performed when primary closure of uninvolved skin was possible. Two patients with stage III disease treated with a modified radical mastectomy, as well as 2 patients with stage IV disease treated with lesser surgery, received postoperative local radiotherapy. All patients with stages III and IV disease received chemotherapy in addition to local treatment of the diseased breast. All patients who lived were followed for at least 40 months (range 40 - 117 months). Of the patients who died, all succumbed to their disease.

### Results

The 20 cases of histologically proven Paget's disease of the breast comprised 9 white and 11 black patients with a mean age of 52.6 years (range 40 - 73 years). The incidence at the breast clinic for this disease was 1.06% (20/1997) over the 12 years.

Histologically, all cases were diagnosed as ductal carcinomas; 3 were reported to be intraductal carcinomas. One of these 3 patients presented with a clinically diagnosed mass and the other 2 with nipple disease only.

Clinically, 20% of the patients presented with a mass only, 60% with both a mass and nipple disease and 20% with nipple disease only. As was to be expected, more patients with a mass (68.75%) had axillary lymph node involvement than patients with nipple disease only (25%). The only patient who presented with nipple disease alone and diseased lymph nodes had, on histological examination, an infiltrating ductal carcinoma. None of the patients with nipple disease alone and in situ lesions had diseased axillary lymph nodes. The cumulative 5-year survival rates for the different clinical groups illustrate that only 22% of the patients with a mass and disease lymph nodes survived 5 years whereas 50% of the patients with negative nodes survived 5 years. All the patients with nipple disease alone survived 5 years.

The cumulative 5-year survival rates for the different TNM-stage groups are illustrated in Fig. 1. Sixty per cent of the cancers could be classified as early lesions (stages I and II) while 40% were late lesions (stages III and IV).

All patients with nipple disease only were alive at 5 years. The 5-year survival rate for patients with stage I and II disease was 83%. No patient in the stage III or IV category survived more than 4 years. Two-thirds of patients in stage I and II category and three-quarters of patients in stage III and IV category presented with both a mass and skin or nipple involvement. Nevertheless, the difference in survival rates between the two categories is clear.

![Fig. 1. Cumulative 5-year survival rates (TNM staging)](image)

### Table I. Treatment According to Stage

<table>
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<th>Stage</th>
<th>No. of patients</th>
<th>Modified radical mastec.</th>
<th>Wide local excision</th>
<th>Local mastec.</th>
<th>Chemotherapy</th>
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<td>Poly Mono None Radiotherapy</td>
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Fig. 1. Cumulative 5-year survival rates (TNM staging)
This, we believe, reflects the relative unimportance of skin or nipple involvement in comparison with tumour size and lymph node involvement as predictors of survival.

Most black patients presented with late disease (83.6%) and most white patients with early disease (88.9%). Of the black patients, 82% presented with both mass and nipple disease, while 9% each presented with a mass or nipple disease alone. White patients were evenly distributed between the three clinical groups, namely 33.3% in each group.

Discussion

The 1.06% incidence of all breast cancers for Paget’s disease is in agreement with that reported in the literature. The histological data also agree with those in the literature, i.e. that Paget’s disease of the breast is mainly a tumour of ductal origin.

To be able to draw firm conclusions regarding tumour biology and treatment of Paget’s disease, a larger series than ours is clearly necessary. However, we feel that certain trends can be detected in our data and that these lead to certain suggestions regarding tumour biology and future treatment policies.

Patients who present with only nipple disease represent the clinically good prognosis group. The reason for this is to be found in the histological data. Nipple involvement only usually represents the in situ form of the disease and so the axillary lymph nodes are usually not involved and thus the prognosis is excellent. Recently, Lagios et al. reported 5 patients with Paget’s disease of the breast who presented with nipple disease alone and who where treated with wide local excision of the nipple-areola and the underlying large lactiferous duct. None of these patients received radiotherapy postoperatively. The follow-up period was 50 months and only 1 patient developed a local recurrence during that period, again illustrating the good prognosis for these patients even with comparatively minor surgery.

It has been documented that Paget’s disease of the breast can be multicentric. Mammography, together with careful clinical examination, can be of help in determining this phenomenon. We believe that when multicentricity is demonstrated, breast-saving surgery should not be performed. On the other hand, if multicentricity is not demonstrated the principles of minor surgery might be applicable to Paget’s disease presenting with nipple disease alone. It would seem reasonable to treat these patients with a wide conal-type excision plus axillary dissection in discontinuity to determine the lymph gland status for prognostic and adjuvant chemotherapy purposes. All patients treated in this way should obviously also receive local radiotherapy to clear the remaining breast of any microscopic malignant foci left in situ.

At present it is accepted in published reports that Paget’s disease of the breast where a mass is present behaves like ordinary breast cancer. Usually the mass represents an infiltrating ductal carcinoma. Our data is in accordance with this knowledge; as could be expected more patients with a mass had positive axillary lymph nodes and therefore the prognosis was poor compared with patients without a mass. The main predictors of prognosis in patients with a mass are therefore the presence of diseased lymph nodes and the tumour size.

It seems as though nipple-areola or skin involvement per se is not of much biological importance in cases presenting with both lesions. We therefore believe that the TNM method of staging can be applied to cases presenting with both lesions and that the nipple involvement (skin lesion) itself does not worsen the prognosis in this context.

The validity of breast-saving surgical treatment in patients presenting with a mass is unclear because of the smallness of the series. Therefore only speculation remains. If we accept that skin or nipple involvement is of no much biological importance then breast saving surgical procedures might also be applicable to small (T1) lesions situated immediately behind the nipple and areola, combined with axillary lymph node dissection and postoperative radiotherapy. Local surgery for T2 lesions in this region of the breast might need resection which leaves not much breast; this may be cosmetically unacceptable to the patient, especially when the breasts are small.

The mainstay of surgical treatment of Paget’s disease of the breast at present is a modified radical mastectomy. A clinical trial to test the abovementioned speculations is clearly needed. Undoubtedly one centre would take many years to provide a valid answer because of the rarity of the disease, therefore a multicentred approach is clearly necessary for such a trial to be completed in a reasonable time.

On first impressions there was a substantial clinical difference between the two racial groups. More black patients presented with a mass and nipple disease than whites. Also more black patients presented with more advanced disease than whites. However, it seems that the difference in the clinical aspect can be found in the difference between the stage at presentation in the two race groups. Possibly because blacks reached our clinic later than whites, their disease had more time to develop into a mass and to invade the nipple as well. It is therefore not possible from our data to determine any racial differences in Paget’s disease of the breast.

References